# imprimis

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# RELEASING THE GENETIC GENIE: HOW RISKY?

**Editor's Preview: What actually goes on at a seminar of the Center for Constructive Alternatives?**

**Leading thinkers from around the world gather *with Hillsdale College* students and faculty for a week of exploring ideas and values in collision. Issues in public policy and ethics are clarified. Genuine liberal arts education—rare on today's vocational-minded, relativist campuses—occurs.**

**Both conservative and liberal viewpoints are presented in the CCA, without labels so students can weigh them on their merits. *Imprimis* this month invites its readers to join in that experience of responsible choice between clashing ideas.**

**Professors Alexander Capron and Liebe Cavalieri were among ten speakers at a CCA seminar on the genetic revolution in March 1983. One's theme was promise; the other's, concern. Which, in your opinion, makes the more liberal argument and which the more conservative? How do their premises differ? Which side do you take?**

## Enormous Potential for Good

By Alexander Capron

Science raises many important issues for society—yet none are more important than those being created by genetic engineering.

Until a few years ago, when a person used that term, he was speaking metaphorically—as a mother would if she said she hoped to "engineer" a marriage between her daughter and a handsome young doctor. Today fact has replaced metaphor. The changes that can be constructed in genes are direct and precise.

In 1965 the term "genetic engineering" was coined for what has come to be a wide range of techniques by which scientists can add genetically determined characteristics to cells that would not otherwise have possessed them.

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## We Do Not Have the Wisdom

By Liebe Cavalieri

The very core of life has been put at man's disposal. What had been a scholarly, reflective science, molecular biology, was transformed, ten years ago, into a force that not only can examine the living organism but now can manipulate it in ways never before possible, at the will of the scientist.

Life systems can be restructured by creating a new architecture for DNA. Living cells of all types can be engineered so that they can perform tasks foreign to their species. Bacteria can be transformed so that they carry out human functions. Cancer viruses can be propagated inside bacteria. Mice can be grown to twice their normal size. Intervention in the germ line (reproductive cells) of mice has been achieved, opening the way for similar procedures in humans.

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im•pri•mis (im-pry-mis) adv. In the first place, from Latin *in primis,* among the first things...

*Imprimis* is the journal of Hillsdale's two outreach programs seeking to foster clear thinking on the problems of our time: the Center for Constructive Alternatives in Michigan and the Shavano Institute for National Leadership in Colorado. A subscription is free on request.

**Alexander Capron**
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In the early 1970s, scientists learned how to isolate specific sequences in the deoxyribonucleic acid (or DNA) from one species and attach this genetic material—"recombinant DNA"—to a different species. The layperson's term "gene splicing" describes the technology well, for like a seaman putting two pieces of rope together, a scientist using the recombinant DNA method can chemically "snip" a DNA chain at a predetermined place and attach another piece of DNA at that site.

My conclusion is that the technique is one with enormous potential for good—but we must look before we leap. There is need for public participation in an explicit process of scrutinizing the ethical and social implications of gene splicing.

Why is gene splicing done? The scientist at the bench will give you the old Hillary-on-Everest answer—it is done because it is there, because the process of gaining the knowledge is so fascinating. And indeed it is—it is elegant and it promises to provide answers to many fundamental issues in biology—from the molecular to the cellular to the evolutionary level.

**About the Authors**

Alexander Morgan Capron recently completed three years' service as executive director of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, which rendered its final report early in 1983. He is currently Professor of Law, Ethics, and Public Policy at Georgetown University.

Liebe F. Cavalieri is Professor of Biochemistry at the Graduate School of Medical Sciences, Cornell University. He has also had a long association with the Sloan-Kettering Institute for Cancer Research. As a researcher, he is credited with pioneering discoveries in the molecular biology of DNA. As a science writer, his publications include the book *The Double-Edged Helix: Science in the Real World*.

The editors extend special thanks to Professors Samuel Townsend, Donald Heckenlively, and Ted Platt of the Hillsdale natural sciences faculty for their invaluable assistance in assembling the CCA seminar on which this issue is based.

Today it is also apparent that gene splicing has many more practical applications—in industry, in agriculture and in medicine. I want to concentrate on the latter—to provide a focus for our discussion because I think it is the application that raises the most interesting questions.

**Medical Applications**

The President's Commission has recently completed a study of the medical applications of genetic engineering. We examined three ways in which gene splicing may enter into the treatment of human beings. Moving from the most near-at-hand and familiar to the most far-off and controversial, they are: the production of useful drugs and biologics, the diagnosis of genetic diseases and the cure of such diseases.

You have probably already heard about the first of these subjects, particularly the use of recombinant DNA techniques to create bacteria capable of producing desirable medical products—like interferon or human growth hormone.

The second area in which gene splicing can be applied in medical care—namely in genetic screening and diagnosis—has also recently begun bearing fruit. This technique holds great promise for genetic disorders or carrier status that until now have not been readily diagnosable because present testing methods look for gene products rather than for the genes themselves.

Potentially, the technique would not only be useful in prenatal and carrier screening for recognized "genetic defects" but also in detecting the presence or absence of genes associated with other conditions or characteristics.

The most novel and important area is in using gene splicing to cure genetic disorders. If this proves possible, it would differ from other treatments because it would not involve the manipulation of the patient or the application (often continually) of a drug but the actual alteration of the cause of the condition itself.

Although treatments of this sort are almost certainly further in the future than other therapeutic uses of gene splicing, they raise much more troubling issues. There are the special ethical problems of creating human beings with the intention of altering them—entirely without their consent. And there are the social and biological concerns over deleterious changes that rather than being limited to one person or one generation would become part of the human genetic inheritance.

**The Frankenstein Factor**

In reviewing statements about gene splicing in the popular press, I have been struck by the frequent invocation of what Willard Gaylin some years ago called the "Frankenstein factor." The analogy is illuminating for several reasons. First, Dr. Frankenstein was a creator of new life and the gene splicers have raised questions about mankind's role as creator. Second, Dr. Franken-

stein's creation was a frightening monster and gene splicing has raised fears about strange new life forms.

The Frankenstein story also reminds us of the tale of the Sorcerer's Apprentice—in both, a development intended to be beneficial proved to be dangerous when it got out of control.

Fourth, the Frankenstein analogy bespeaks people's concern that something is being done to them and their world by individuals concerned with their own goals but not necessarily with human betterment. As C. S. Lewis once observed, "Man's power over nature is really the power of some men over others with nature as their instrument."

But most particularly, it seems to me that the Frankenstein story was on the lips of many people—both scientists and lay people—because it dealt with the creation of a new being with a human form.

Like the new knowledge associated with Copernicus, Darwin, Freud, and Einstein, that associated with the gene splicers offers further challenge to human beings' conception of themselves as the unique and even sacrosanct center of the universe. By identifying DNA and learning how to manipulate it, science seems to have reduced people to a set of malleable molecules that can be interchanged with those of species that people regard as inferior.

And unlike the earlier revolutionary discoveries, those in molecular biology are not merely descriptive; they give scientists vast new power for action. The use of this new power has frequently been labelled "playing God." This description carries with it an implication that it is wrong for human beings to engage in this activity at all—that we have overreached ourselves by pretending to have God-like powers.

This objection has several possible meanings. At least one is not persuasive. For millenia, people have interfered with nature both intentionally and unintentionally as a side effect of other human activities. There is some difference in aspects of gene splicing, however, that might create hybrids that are capable of reproducing themselves—but here the concern would not be that crossing species lines is inherently wrong, merely that if the effects are deleterious their harm may be multiplied by their perpetuation into later generations—like a recombinant DNA Dutch elm disease. This is an issue that deserves to be treated with great care, but it is not one that raises a problem of principle.

There is, however, another aspect to the complaint about "playing God" in crossing species lines where a prohibition may be in order, and that is in the hybridization of human beings with other living things.

The prospect of creating an actual being with partially human characteristics offends a deeply held taboo. There is, however, no legal or regulatory prohibition of such a step. And if the barrier is to survive in the face of scientific advances, the reasoning behind it will need further attention. It may, for example, be fruitful to clarify what it is about human beings that is unique—whether it is the sum of their characteristics or the possession of particular characteristics. There is a certain irony here since a person approaching the subject from a religious or philosophical position is likely to deny that human beings are simply a reflection of the particular chemicals that make them up, and yet the objection being raised is to an alternation in those chemicals.

When one moves from absolute prohibitions on the human uses of gene splicing to questions of particular consequences, one is faced immediately with a realization of the great uncertainty in this field.

The concern for personal health has several bases. One is the notion that in replacing a particular DNA sequence that is regarded as deleterious, a physician might also unintentionally be removing other genetic material that is in fact beneficial. Moreover, even when only a particular gene is replaced there is a risk that some advantage supplied by the gene may be lost. Little is known about the range of effects a single gene can have; many affect several parts of the body in what appear to be a wide variety of ways.

The possibility that genetic changes would be inherited also raises many questions. For example, would such alternations be so widespread in society that the gene pool would lose desirable diversity, thereby exposing mankind—like some inbred strain of rice or corn—to the risk of decimation by a newly arising pathogen?

**Social Questions**

In addition, the ability to change one's genes challenges the basic assumptions about people's links to, and responsibility for, their progeny. In some ways, one's responsibility may be increased: Will it be acceptable for people simply to take the results of the natural lottery by which characteristics are now determined, or will responsible parents be expected to "correct" bad genes and to augment others to give their children an opportunity for a higher level of physical or cognitive functioning?

On the other hand, knowing that future generations may employ an even more advanced technology to alter or to replace characteristics passed on to them may weaken people's sense of genetic continuity. Furthermore, by blurring the line between what counts as a serious defect or disability and what is "normal functioning," gene splicing may alter our perception of what society owes to children, particularly those burdened by handicaps.

The potential of gene therapy or surgery to improve functioning calls into question the scope and limits of a central element of a democratic political theory: the commitment of equality of opportunity. Would genetic

engineering become mandatory—along, perhaps, with restrictions on natural reproduction—in order to avoid the effects of the natural lottery that has such a profound influence on our opportunities in life?

Any discussion of equality leads naturally into a discussion of justice. Who should decide which line of genetic engineering ought to be pursued and which applications of the technology to which patients ought to be undertaken? This is a question that seldom arises about medical progress. Decisionmaking in medicine is widely dispersed, resting upon the tripod of peer standards, patient consent, and very broad and general state regulation. But if genetic engineering comes to be seen as a very beneficial and powerful form of treatment, questions will certainly be raised about access to it not only in the use of techniques that have been developed but also in deciding about which areas need to be pursued.

It seems to me that this issue lies behind the concerns that have been expressed by many about the effect of commercial involvement in the basic research carried on by academic and other independent institutions and about the effects of such control on the availability of dispassionate expert advice for policymakers.

Although the Commission found that the issues raised by gene splicing in human beings can better be taken into account by biomedical scientists, government officials, and the public if they are considered individually, it would be a mistake to respond to the new technology solely by reducing all concerns to assessments of particular consequences or applications.

Even after the potential consequences have been carefully sifted and their implications for human welfare have been explored, there remains an important residual concern expressed by the warning against "playing God." It reminds human beings that they are only human and will some day have to pay if they underestimate their own ignorance and fallibility.

At this point in the development of genetic engineering no reasons have been found for abandoning the entire enterprise—indeed, it would probably be naive to assume that it could be. To expect humanity to turn its back on what may be one of the greatest technological revolutions may itself betray a failure to recognize the limits of individual and social self-restraint.

Assuming that research will continue somewhere, it seems more prudent to encourage its development and control under the sophisticated and responsive regulatory arrangements of this country, subject to the scrutiny of a free press and within the general framework of democratic institutions.

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**Liebe Cavalieri**
*(Continued from page 1)*

We can anticipate that recombinant DNA technology will present problems that are as pervasive and disquieting as those that have sprung from nuclear fission. Both are major scientific accomplishments that confer a power on humans for which they are psychologically and morally unprepared. The physicists have already learned this, to their dismay; the biologists, not yet.

Nobel laureate David Baltimore has recently proclaimed: "We can outdo evolution"—a signal that molecular biologists are about to translate genetic engineering into an instrument of power, much the way the physicists did when they exploited their discoveries at the beginning of the nuclear age.

**Economic Demands vs. Human Needs**

In the habitual manner of our times, scientists are pursuing their interests and then rationalizing the pursuit by looking for uses for their discoveries, whether society needs them or not, rather than starting with the most pressing problems and looking for solutions. This may have been acceptable in the past but I'm not sure society can afford this luxury right now, when it is facing an alarming series of threats that have recently become apparent.

These threats include water and air pollution by industrial products and wastes, accelerating soil erosion and desertification, exhaustion of renewable resources such as water and forests faster than they can be replenished, the "greenhouse" effect, acid rain, ozone depletion, species extinction, depletion of mineral resources, excessive population growth, malnutrition—not to mention the nuclear arms race.

These are not separate problems; all are interrelated, and in the long run they are exacerbated by the fact that solutions are sought on an individual basis, with no regard for the consequences that any given "solution" might have for other members of the set. Too often, economic demands are pitted against human needs.

Recombinant DNA technology has been so widely promoted by scientists and the news media that industrial giants from all over the world have been induced to invest heavily in it. Genetic manipulation of micro-organisms by the new techniques has proceeded rapidly and is now widespread. More than 150 genetic engineering firms mainly oriented just now toward the design of industrially useful micro-organisms, have formed in the last few years. The technology has been translated into economic power, and with it molecular biologists have become entrepreneurs, leaving the Ivory Tower far behind.

The profound ecological, social, and ethical implications of genetic engineering have been obscured by its marketability. All forms of life are vulnerable to this

technology—any DNA can be connected to any other DNA; human DNA can be put into viruses and bacteria and vice versa; cancer virus DNA has already been put into bacteria, and so on. The gene pool of the Earth, the life-determinant of the future, is the experimental subject for genetic engineering. This precious, irreplaceable legacy of natural evolution is in the truest sense a one-time occurrence, and it would be naive to assume that we can manipulate it without harming ourselves. We do not have the requisite infinite wisdom.

### Delicate Mechanism

In the face of the infinite complexity of natural systems, the idea that we could improve on the design of nature is not only hubris, it is frightening. In Lewis Thomas's words, we are ignorant "most of all about the enormous, imponderable system of life in which we are embedded as working parts. We do not really understand nature at all." We know that the Earth behaves like an indivisible, delicately tuned mechanism, in which the inanimate environment is strongly conditioned by living things, and vice versa; but we have only begun to decipher the influence of each part on the whole.

For example, we recognize that certain microorganisms convert organic wastes to usable nutrients, and that this recycling process is critical in maintaining the composition of the atmosphere and other conditions favorable to human life and to the web of species that sustain us. But we cannot predict the effects on these vital microorganisms of accelerated evolution, engineered by man, coupled with the accelerated environmental changes now produced by human activities.

However, as the result of current efforts to design industrially useful organisms, microorganisms with properties taken from higher forms of life will inevitably escape into the ecosphere; other engineered forms will eventually be released intentionally into the environment for purposes such as the solubilization of trace metals in mining operations or the digestion of oil spills. We are laying the groundwork for unforeseen evolutionary changes that may create an environment inhospitable to present species.

Frequently, one is confronted with specious arguments about how well evolutionary forces have managed thus far and how they will continue to provide viable ecosystems. Certainly, we can find some assurance in nature's resiliency; life has survived environmental upheavals for millions of years. But as conditions have changed, so has the balance of life, with incompatible forms disappearing and new ones arising. If there were a drastic change in the environment, some forms of life would undoubtedly adapt, but humans, with their many, exacting biological requirements, could not evolve fast enough to become compatible with the new environment.

Genetic engineers have many visions. They plan to introduce foreign genes into crop plants in the hope of solving the problem of world hunger. But food experts and agronomists recognize that enough is already produced to feed everyone in the world. Distribution is the problem; it is not scientific but rather economic and political.

It is obvious that it would be naive to attempt to solve the food problem with recombinant DNA technology. Even if that technology should someday succeed in producing plants that can fix atmospheric nitrogen, the most that could be hoped for would be a small contribution of a temporary respite—a technological fix that has no bearing on the fundamental population problem and might have adverse side effects that would exacerbate the situation by producing ecological instability.

Bacterias that will consume oil from oil spills on the oceans have already been produced. In addition to ecological questions, the social implications of this procedure are far-reaching. It has been shown that crude oil spilled from faulty tankers has an adverse effect on marine life. The application of vast numbers of bacteria to consume the spill would doubtlessly lead to mutant forms with an altered metabolism, so that some might find a niche in the oceans or even on land, causing ecological disturbances.

### 'When Do We Start?'

Genetic engineers have not overlooked the possibility of changing man himself. It will not be long before single-gene replacement therapy—the correction of a defective gene—will be possible. Although in this case the change will die with the patient, more radical experiments are underway in which eggs or sperm are altered to produce individuals with hereditary alterations. Considerable success along these lines has already been achieved in mice.

The rationale for these experiments is that they provide information about mammalian genetics and fetal development. But when the technology for intervention in human evolution has been perfected, will it remain unused? Preliminary experiments with human embryos have been underway in England, for example, for several years. What is more seductive than the power to design human beings?

Although the repair of genetic defects appears laudable, the indistinct boundary between repair and improvement raises serious problems. Who is to decide what qualities define a perfect human? In a changing world, the genetic engineering of perfection would imply a divine intelligence that could peer far into the future. There are some scientists who think they have such power. Professor James Bonner of Cal Tech has recently suggested:

> The logical outcome of activities in modifying the genetic make-up of man is to reach the stage where couples will want their children to have the best possible genes. Sexual procrea-

> tion will be virtually ended. One suggestion has been to remove genetic material from each individual immediately after birth and then promptly sterilize that individual. During the individual's lifetime, record would be kept of accomplishments and characteristics. After the individual's death, a committee decides if the accomplishments are worthy of procreation into other individuals. If so, genetic material would be removed from the depository and stimulated to clone a new individual. If the committee decides the genetic material is unworthy of procreation it is destroyed.... The question is indeed not a moral one but a temporal one—when do we start?

Such men have fallen into the trap that often stands between scientists and the realization of a mature social conscience: reductionism, the operational form of modern scientific research. It requires that the system under investigation be first separated into its most minute components. The forest as a whole may thereby pass unnoticed.

This is a common pattern in our society. The focus is on specific and immediate problems, considered individually and in isolation from life as a whole. It is inevitable under these circumstances that the chosen solution to one problem will exacerbate another. Long-range social and economic well-being can never be attained by systematically ignoring the interrelatedness of our problems and the side effects and more distant consequences of our decisions; this fragmented approach is condemning us to crisis after crisis.

The Global 2000 Report to the President, which appeared in 1980, is a stark testimony to this. The report projects that if we continue on the same path, "the world in the year 2000 will be more crowded, more polluted, less stable ecologically, and more vulnerable to disruption than the world we live in now. Despite greater material output, the world's people will be poorer in many ways than they are today." The report calls for "new initiatives, if worsening poverty, human suffering, environmental degradation and international tension and conflicts are to be prevented. There are no quick fixes. New and imaginative ideas—and a willingness to act on them—are essential."

Insofar as the scientific community has been distinguished by the purity of its motivation and its lack of bias and self-interest, to that same extent it has been free of corrupting power. But today power is thrust upon the scientist by the comprehensive knowledge he has gained, as well as by the vast technological influence of science in our society. To be true to itself, science must reject power in favor of responsibility. The scientist must have a conscience. Hand wringing after the fact offers no solution, as we have learned from the nuclear experience.

The discoveries that energy can be released from the atomic nucleus and that DNA, the material of the cell nucleus, is the genetic stuff of life are without parallel in human experience. These twin scientific feats, one at the core of matter, the other at the core of life, demand a new consciousness if human life on this planet is to continue.

We have mismanaged the applications of the first discovery. Now, as the second is about to be exploited, we must not permit the biosphere, surpassing as it does our understanding, to become an experimental subject. There is only one Earth, one earthly biosphere, and we are part of it. There is no margin for error.

## "Pause for the Pledge" Planned Nationally on Flag Day, Tuesday, June 14, at 7:00 p.m. EDT

**Many of us at Hillsdale College in Michigan and the Shavano Institute in Colorado will join the national moment of honor to the American flag on the evening of June 14, Flag Day.**

**We encourage friends throughout the country to pause wherever you are that day at 7:00 p.m. Eastern Daylight Time (6:00 p.m. Central, 5:00 p.m. Mountain, 4:00 p.m. Pacific) and recite the Pledge of Allegiance with us.**

**"Pause for the Pledge" has gained widespread grassroots support since it was originated in 1980 by the National Flag Day Committee in Baltimore. Participation now reaches into all 50 states and various U.S. overseas territories. The governors of 36 states have recognized the observance with proclamations, and endorsement by Congressional resolution is pending.**

**Organizers hope that the number of Americans who "pause for the Pledge" at 7:00 p.m. EDT this June 14 will be several times as many as the estimated 12 million who marked the event a year ago. For all who love Old Glory and "the Republic for which it stands," here is a simple yet stirring way to say so.**

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